March 7, 2002

Ronald L. Joiner, Ph.D.
General Electric Company
One Plastics Avenue
Pittsfield, MA 01201

Dear Dr. Joiner:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Isodecyl/Phenyl Phosphite Chemical Category, posted on the ChemRTK Web Site on, October 11, 2001. I commend the General Electric Company for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Chemical RTK HPV Challenge Program website EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the attached Comments on the Chemical RTK web site within the next few days. As noted in the comments, we ask that the General Electric Company advise the Agency, within 90 days of the posting on the Chemical RTK website, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit general questions about the HPV Challenge Program through the Chemical RTK web site comment button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@.epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Attachment

cc: W. Sanders
A. Abramson
C. Auer
M. E. Weber

EPA Comments on Chemical RTK Challenge Submission:

Isodecyl/Phenyl Phosphite

SUMMARY OF EPA COMMENTS

The sponsor, General Electric Company, submitted a test plan and robust summaries to EPA for the Isodecyl/phenyl phosphite category dated September 11, 2001. EPA posted the submission on the ChemRTK HPV Challenge Web site on October 11, 2001. The isodecyl/phenyl phosphite category includes triphenyl phosphite; isodecyl diphenyl phosphite; diisodecyl phenyl phosphite; and triisodecyl phosphite.

EPA has reviewed this submission and has reached the following conclusions:

1. Category Justification. The submitter's support for grouping the chemicals under this category is acceptable.

2. Physicochemical and Environmental Fate Data. The submitter's approach for these endpoints is acceptable for the purposes of the HPV Challenge Program. However, the submitter should provide measured vapor pressure data, at a minimum, for triphenyl phosphite.

3. Health Endpoints. EPA agrees with the submitter's proposal to conduct combined repeat-dose/reproductive/developmental toxicity screening tests on two outside members of the category. The acute toxicity and mutagenicity endpoints have been adequately addressed and no further testing is necessary for the purposes of the HPV Challenge Program.

4. Ecotoxicity. The submitter's plan for ecotoxicity testing is acceptable for the purposes of the HPV Challenge Program. EPA suggests that, to address volatility and stability in water concerns, all testing be done with measured concentrations in a flow-through and closed system. In addition, for the test data submitted, test substance purity needs to be reported for proper evaluation.

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.

EPA COMMENTS ON ISODECYL/PHENYL PHOSPHITE CATEGORY CHALLENGE SUBMISSION

Category Definition

The submitter has proposed a category covering the phosphite esters, triisodecyl and triphenyl phosphite, and products containing mixed isodecyl/phenyl phosphite esters. The category is based on a "common functional group (phosphite ester), the successive change across the series from alkyl to aryl esters, and the similarity in manufacturing process and expected breakdown/hydrolysis products." The commercial grade of triisodecyl and triphenyl phosphites is typically >98%. The mixed esters, diisodecyl phenyl phosphite and isodecyl diphenyl phosphite, constitute 50-70% of the commercial product, with lesser amounts of the triisodecyl and/or triphenyl phosphites also present. These substances are covered under the following chemicals: triisodecyl phosphite (CAS No. 25448-25-3); diisodecyl phenyl phosphite (CAS No. 25550-98-5); isodecyl diphenyl phosphite (CAS No. 26544-23-0); and triphenyl phosphite (CAS No. 101-02-0). The category definition is clear and unambiguous.

Category Justification

The submitter bases the category on three criteria: "a common functional group," "common precursors and/or breakdown products," and an "incremental and constant change across the category." All the compounds in the category contain the common phosphite ester functional group, and the ester hydrolysis products are phosphorus acid, isodecyl alcohol, and phenol, in relative ratios equivalent to their respective starting esters.

Structurally, the alkyl:aryl ester ratio of the category members varies incrementally across the group (i.e., 3:0, 2:1, 1:2, and 0:3 for triisodecyl, diisodecyl phenyl, diphenyl isodecyl, and triphenyl phosphites, respectively).

The submitter states that toxicities will increase incrementally with either increasing numbers of phenyl groups in the esters or increasing amounts of residual triphenyl phosphite in the substance that remains after manufacturing. The data from the mammalian toxicity studies do not provide strong support for such a progressive increase. The acute oral and dermal toxicity data suggest that triphenyl phosphite is slightly more toxic than the other members of the category, while the category members containing isodecylphenyl residues have approximately similar toxicity. Although the acute inhalation data indicate low toxicity for all four category members, the LC50 values (>12.6 to >6.4 mg/L) indicate the maximal attainable concentration of each compound, not toxicity. Although the submitter's contention that toxicity varies predictably with phenyl groups/residual triphenyl phosphite is not strongly supported by the data submitted, the data do provide limited evidence that all members of this category have approximately the same degree of toxicity, with triphenyl phosphite possibly being slightly more toxic. This potential similarity in toxicity would be adequate justification that, toxicologically, these chemicals can be included in a single category.

It is difficult to determine whether the ecotoxicity data support the progressive toxicity argument; a trend cannot be identified because the data are limited. Nonetheless, the submitter plans testing for those members without data so that all members will have adequate testing.

Test Plan

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

The submitter's approach for these endpoints is acceptable for the purposes of the HPV Challenge Program. However, the submitter should provide measured vapor pressure data for at least triphenyl phosphite, and not calculated, as proposed in the test plan. OECD guideline 104 states that calculated values may be acceptable if the calculated value is less than $1x10^{-5}$ kPa. The value for triphenyl phosphite is slightly greater than the cutoff value and therefore should be measured. As a general matter, measured physicochemical values are preferred because calculated values may introduce uncertainties that then become magnified in modeling applications.

Environmental Fate (Photodegradation, Stability in Water, Biodegradation, Fugacity).

The submitter's approach for these endpoints is acceptable for the purposes of the HPV Challenge Program. The stability in water tests should be done at environmental pH, and identify the rate of hydrolysis and by-products to inform the aquatic toxicity testing.

Health Effects (acute toxicity, repeat dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

There are adequate data for all four members of the category for acute toxicity, bacterial mutagenicity, and *in vivo* chromosomal aberrations. The submitter has proposed a test for *in vitro* mammalian cell mutations and combined repeated dose/reproductive/developmental toxicity tests. The submitter states that "the pattern of less toxic to more toxic is quite evident as the number of phenyl groups increases," and hence proposes that the "outside members" of the category be tested, while the toxicity of the "interior members" will be extrapolated from the results obtained. If the results obtained from testing the "outside members" are significantly different, then testing "will be conducted on one or both of the interior materials." As indicated previously, the data provided in the test plan do not provide strong support for the contention that there is a pattern of increasing toxicity with increasing number of phenyl groups; however, the proposed testing strategy should adequately address the endpoints for this category. If the "outside members" that

are the structural extremes of the category (i.e., containing either three phenyl or three isodecyl groups) have similar toxicity, then it would be reasonable in this case to extrapolate data to the intermediate members of the category, and if the toxicities are different, the submitter proposes appropriate testing of the "interior" substances. Thus, EPA considers the testing strategy justified by the structural progression of the category members and the relatively flat toxicity data rather than the submitter's purported pattern of increasing toxicity with increasing phenyl groups.

Acute Toxicity.

The submitter's conclusion that no further acute toxicity testing is required is supported by the existing data provided in the submission.

Repeated Dose, Reproductive, and Developmental Toxicity.

EPA agrees with the test plan to conduct combined repeated-dose/reproductive/developmental toxicity screening tests for triisodecyl phosphite and triphenyl phosphite, with additional testing for the other members of the category if indicated by the results obtained from the initial testing.

Genetic Toxicity.

Adequate data are available for this endpoint and no further testing is necessary.

Ecotoxicity

The submitter proposes to conduct the acute base set testing on fish (OECD Test Guideline 203), algae (OECD Test Guideline 201), and daphnids (OECD Test Guideline 202) for the two category members that do not have submitted data (triphenyl phosphite and triisodecyl phosphite). The additional testing will support the existing adequate data.

All tests should use closed systems and mean measured concentrations to address volatility and stability in water concerns. Testing of these chemicals should follow the Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures (http://oecd.org/ehs/test/monos.htm).

Fish.

Adequate data are available for this endpoint for diisodecyl phenyl phosphite and isodecyl diphenyl phosphite.

Invertebrates.

Adequate data are available for this endpoint for diisodecyl phenyl phosphite and isodecyl diphenyl phosphite.

Algae.

Adequate data are available for this endpoint for diisodecyl phenyl phosphite and isodecyl diphenyl phosphite.

Specific Comments on the Robust Summaries

Ecotoxicity

Test substance purity was consistently missing from the robust summaries and needs to be provided so that the ecological toxicity of these substances can be accurately characterized.

Followup Activity

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.